**Supplementary figure legends**

**Figure S1: VEGFR2 expression and FGF signaling. A.** VEGFR2 expression is downregulated in primary mouse endothelial cells lacking FGF signaling: mouse aortic endothelial cells (MAEC) were transduced with Ad-GFP or Ad-FGFR1DN and total cell lysates were subjected to Western analyses. NT denotes no transduction. **B.** Quantitative real-time PCR analysis of total RNA isolated from BAEC transduced with either Ad-Null or Ad-sFGFR1-IIIc. Data shown as mean±SD, n=3, *: $P<0.05$. **C.** FGF receptor trap decreases VEGFR2 levels: Western analysis of VEGFR2 expression in BAEC exposed to sFGFR1-IIIc (FGF-trap) or control virus. **D**. Effect on FRS2 knockdown on VEGFR2 expression: Western analysis of HUAEC treated with FRS2α shRNA or control construct. **E**. Quantitative real-time PCR analysis of total RNA isolated from mouse lung microvascular endothelial cells (MLEC) transduced with either Ad-Null or Ad-FGFR1DN. Mean±SD, n=3 mice/group, *: $P<0.05$. **F.** Quantitative real-time PCR analysis of total RNA isolated fromMLEC transduced with either Ad-Null or Ad-sFGFR1-IIIc. Mean±SD, n=3 mice/group, *: $P<0.05$. **G.** Western analysis of MLEC transduced with Ad-FGFR1DN or Ad-Null.

**Figure S2: *VEGFR2 half-life*. A**. Western blotting of total cell lysates from BAEC transduced with Ad-GFP or Ad-FGFR1DN and treated with 10 μg/ml cycloheximide for up to 3 hours. **B.** Quantitative analysis of Western blotting from 3 independent experiments described in A. The value at time point 0 is designated as 1. **C**. Western blotting of total cell lysates isolated from BAEC transduced with Ad-GFP or Ad-FGFR1DN and treated with different doses of MG132 for 3 or 6 hours.

**Figure S3: Signaling pathways regulating VEGFR2 expression. A.** Inhibition of Erk1/2 leads to a reduction of VEGFR2 expression: Western blotting of total cell lysates isolated from BAEC treated with 10 μM U0126 in the normal growth medium for the indicated period of time. **B**. Quantitative analysis of VEGFR2 levels based on 3 independent experiments described in A. The value at time point 0 is shown as 1. Mean±SD, * $P < 0.05$, ** $P < 0.01$. **C.** Western blotting of total cell lysates from BAEC treated with 10 μM LY294002.

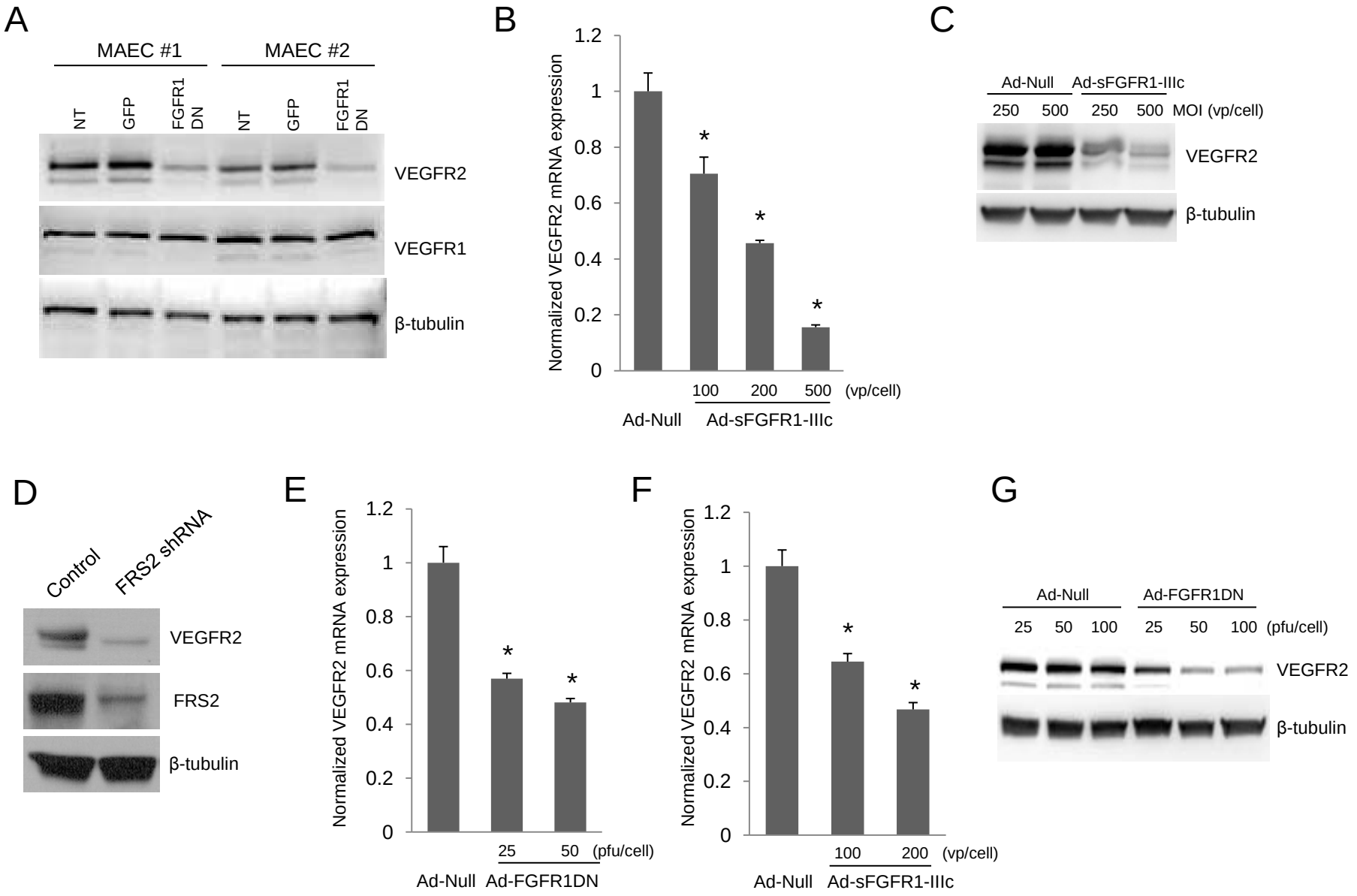
**Figure S4: Ets factors involvement in VEGFR2 expression A.** ChIP assay showing binding of Ets1 and Etv2 to the VEGFR2 enhancer of MS-1 cells. MS-1 cells, either untransfected or transfected with Ets1 or Myc-tagged Etv2, were subjected to ChIP assay. Input DNA, sample representing total input chromatin (1 %). **B.** Western analysis showing reduced pT38 Ets1 in BAECs transduced with Ad-FGFR1DN (MOI: 50 pfu/cell). **C**. Western analysis showing reduced pT38 Ets1 in BAECs treated with 10μM U0126.

**Figure S5: Effect of FGF signaling suppression on angiogenic profile.** MLEC were transduced with either Ad-Null or Ad-FGFR1DN and gene expression was analyzed using mouse angiogenesis PCR array. **A.** Genes downregulated by FGF inhibition. **B.** Genes upregulated by FGF inhibition. **C.** Genes with unchanged expression (less than 2-fold increase or decrease).

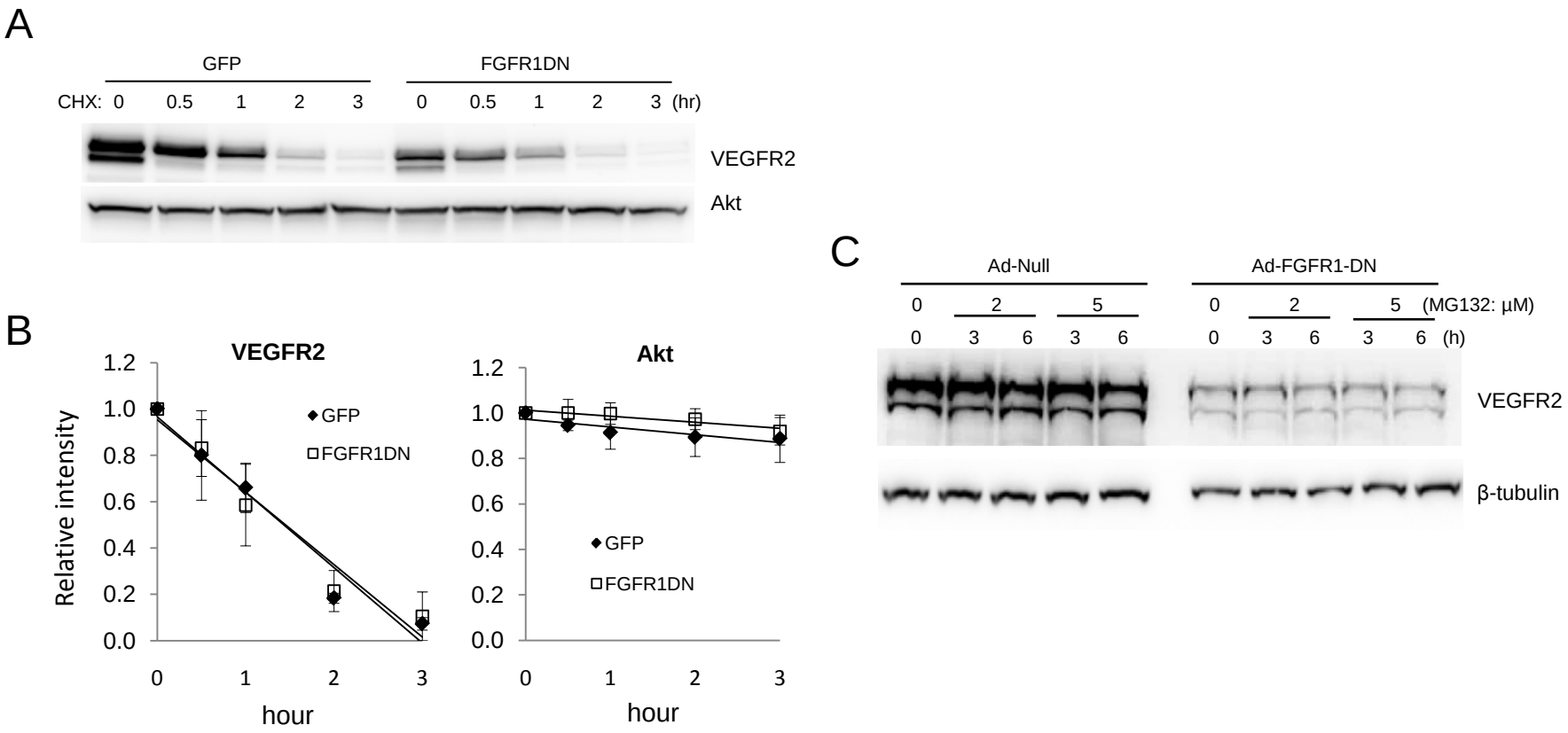
**Figure S6: Validation of the tet-off system. A**. In vitro assay: GFP or pBI-G-FGFR1DN plasmid was transfected in the MEF-3T3 cell line which stably expresses tTA. The pBI-G plasmid vector has a bi-directional Tet-responsive promoter which controls the expression of β-

galactosidase and the gene of interest. After the transfection, cells were treated either with or without doxycycline (2 μg/ml) for 48 h, and the cell lysates were measured for β-galactosidase activities. Mean±SD, n=3 in each group, * : P<0.05 by Student's t-test. Inset: expression of FGFR1DN probed with an anti-HA antibody. **B.** Restricted expression of FGFR1DN in the vasculature of ischemic muscle. Hindlimb ischemia was induced in FGFR1DN mice, and 48 hours later gastrocnemius muscle from ischemic (right) or non-ischemic (left) leg was harvested and subjected to immunostaining for CD31 (red) and HA-tag (green). Bar, 10μm. **C**. Ischemia-dependent expression of FGFR1DN. After removal of doxycycline from diet, FGFR1DN and control mice were subjected to hindlimb ischemia. Gastrocnemius muscle of the ischemic leg was harvested at indicated time points and Western blotting was performed using an anti-HA-tag (upper) or actin (lower) antibody. **D**. Measurement of tissue cGMP levels after hindlimb ischemia. Gastrocnemius muscle was harvested at indicated time points after hindlimb ischemia and cGMP levels were measured. Mean±SD for n=4 mice/group, *: $P<0.05$, **: $P<0.01$.

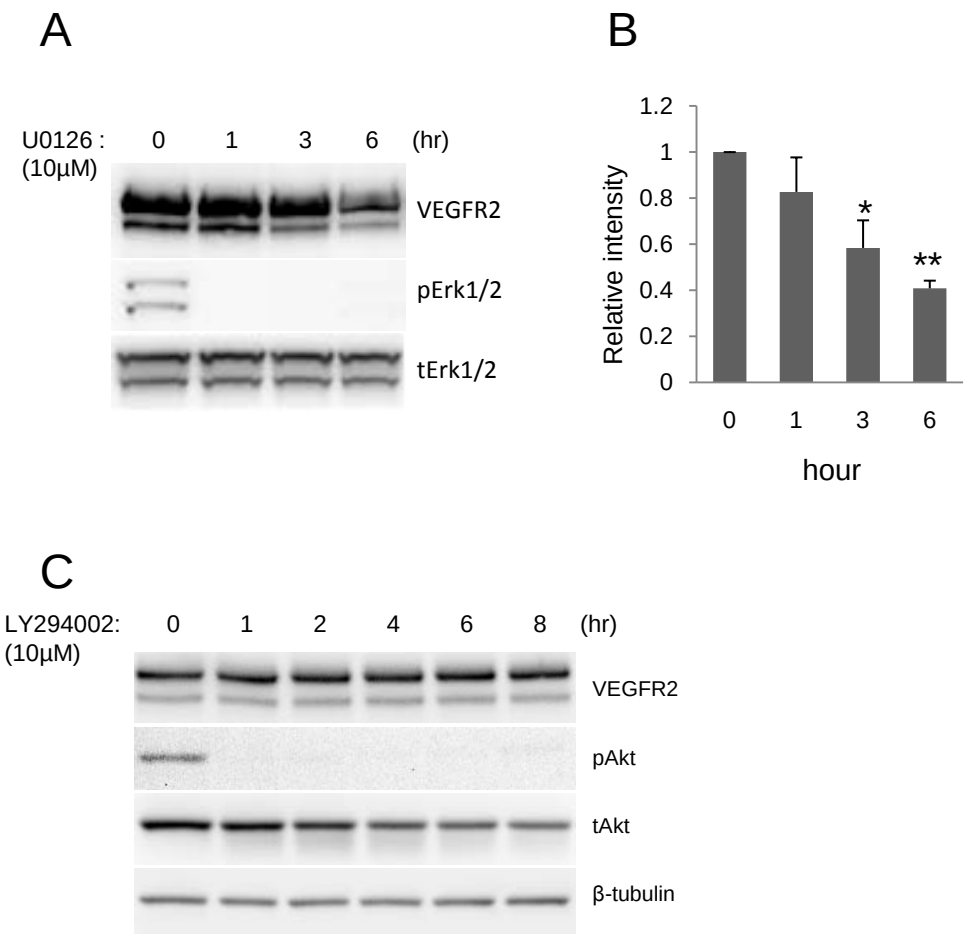
**Figure S7: Evaluation of inflammatory response associated with new vessel formation in mice lacking FGF signaling. A.** Sections of Matrigel plugs harvested from control or sFGFR1-IIIc mice were stained for CD31 and CD45. Bar, 50μm. **B.** CD45 positive area was quantified. Data shown as mean±SD for n=3 mice/group, *: $P<0.05$. **C.** Hindlimb ischemia was induced in control and FGFR1DN mice, and 72 hours later adductor muscle of the ischemic (Rt) and non-ischemic (Lt) leg was harvested and subjected to immunostaining for CD31 and CD45. Bar, 50μm. **D.** CD45 positive area was quantified. Data shown as mean±SD for n=3 mice/group.




Supplementary Figure 1

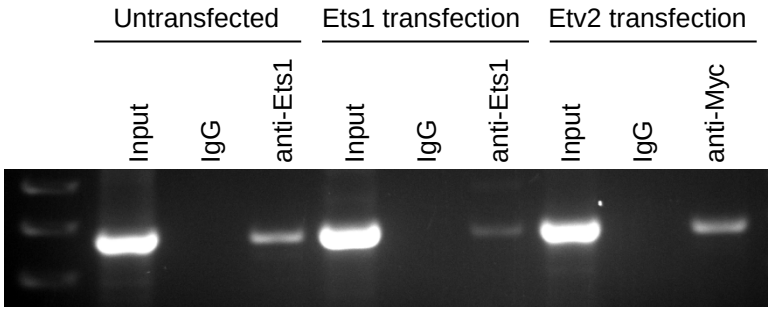



Supplementary Figure 2




Supplementary Figure 3

A

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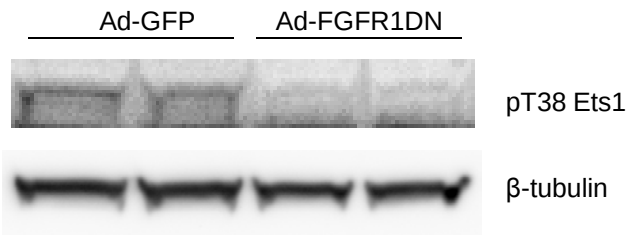


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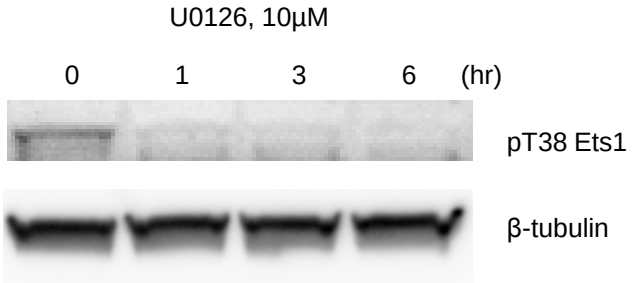



Supplementary Figure 4

A

| Gene Symbol | Fold change sFGFR1-IIIc/Control | Fold up- or down-regulation sFGFR1-IIIc/Control |
|---|---|---|
| Csf3 | 0.06 | -17.31 |
| Bai1 | 0.14 | -7.39 |
| Ccl11 | 0.14 | -7.39 |
| Col4a3 | 0.14 | -7.39 |
| Cxcl5 | 0.14 | -7.39 |
| Tymp | 0.14 | -7.39 |
| Egf | 0.14 | -7.39 |
| F2 | 0.14 | -7.39 |
| Fgf6 | 0.14 | -7.39 |
| Hand2 | 0.14 | -7.39 |
| Il1b | 0.14 | -7.39 |
| Lect1 | 0.14 | -7.39 |
| Lep | 0.14 | -7.39 |
| Plxdc1 | 0.14 | -7.39 |
| Sphk1 | 0.14 | -7.39 |
| Tbx4 | 0.14 | -7.39 |
| Timp1 | 0.14 | -7.39 |
| Tmprss6 | 0.14 | -7.39 |
| Tnf | 0.14 | -7.39 |
| Il6 | 0.16 | -6.27 |
| Angpt1 | 0.17 | -5.84 |
| Plau | 0.21 | -4.83 |
| Tgfb1 | 0.23 | -4.38 |
| Kdr | 0.3 | -3.32 |
| Itgb3 | 0.35 | -2.85 |
| Efna1 | 0.36 | -2.8 |
| Col18a1 | 0.4 | -2.5 |
| Mmp9 | 0.42 | -2.37 |
| Plg | 0.44 | -2.29 |

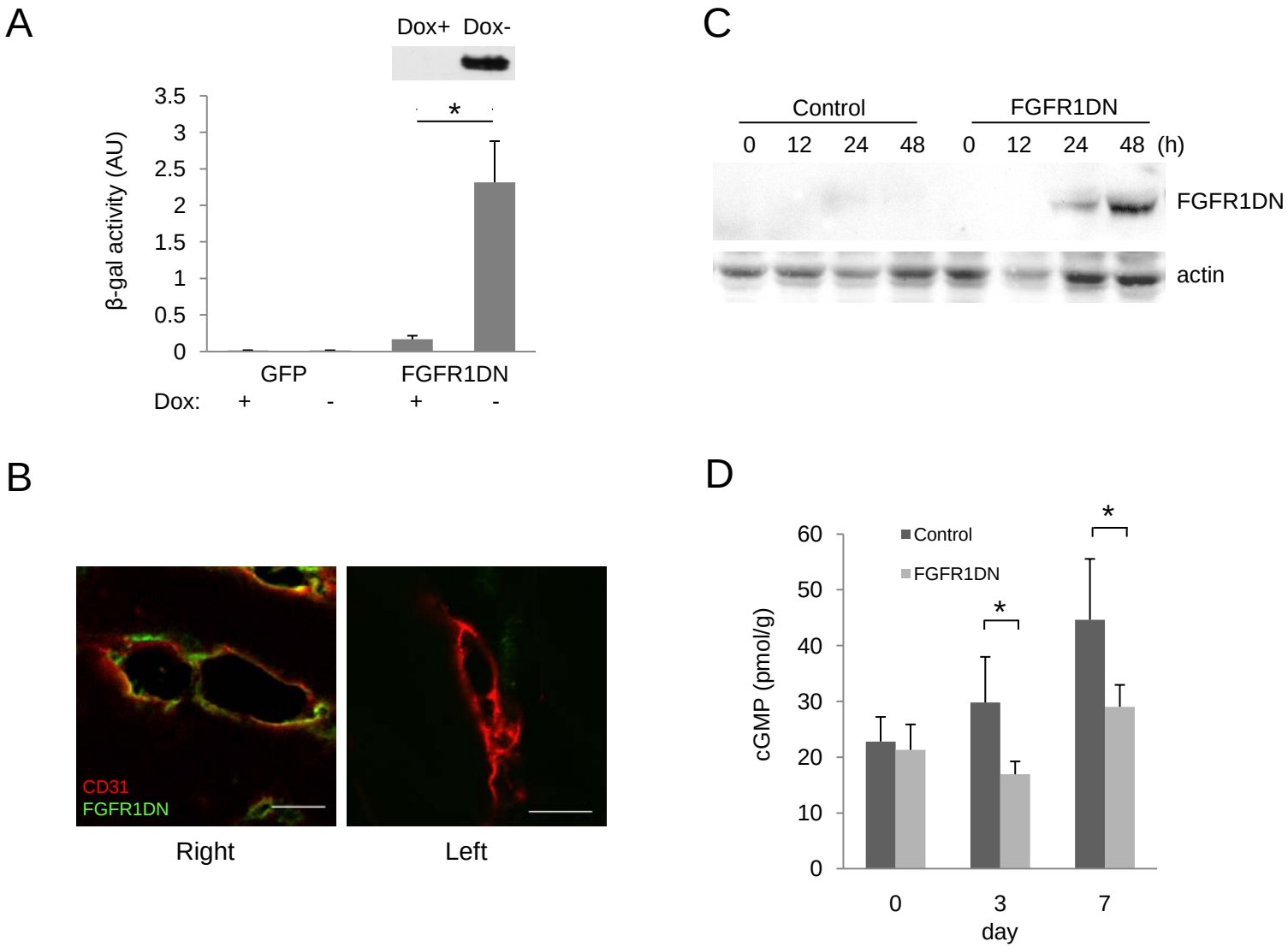
B

| Gene Symbol | Fold change sFGFR1-IIIc/Control | Fold up- or down-regulation sFGFR1-IIIc/Control |
|---|---|---|
| Tnfsf12 | 2.08 | 2.08 |
| Fzd5 | 2.28 | 2.28 |
| Ctgf | 2.45 | 2.45 |
| Tbx1 | 2.68 | 2.68 |
| Mmp19 | 2.72 | 2.72 |
| Igf1 | 3.3 | 3.3 |
| Tgfb2 | 3.36 | 3.36 |
| Cxcl1 | 3.51 | 3.51 |
| Flt1 | 4.55 | 4.55 |

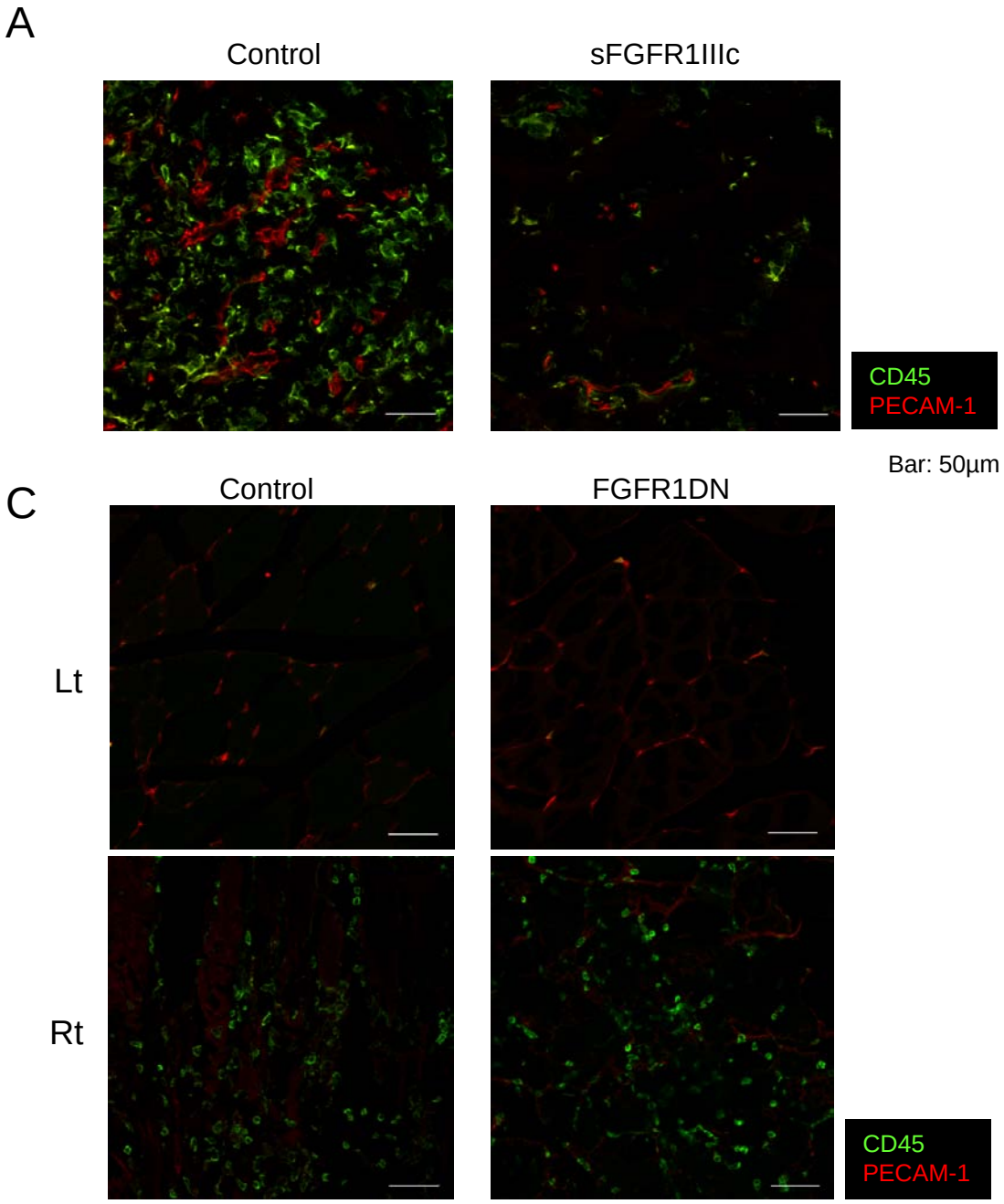
C

| Gene Symbol | Fold change sFGFR1-IIIc/Control | Fold up- or down-regulation sFGFR1-IIIc/Control |
|---|---|---|
| Angpt2 | 0.51 | -1.97 |
| Fgf2 | 0.52 | -1.92 |
| Stab1 | 0.56 | -1.79 |
| Nrp2 | 0.6 | -1.67 |
| Cdh5 | 0.6 | -1.66 |
| Serpinf1 | 0.6 | -1.65 |
| Mdk | 0.62 | -1.61 |
| Itgav | 0.67 | -1.5 |
| Jag1 | 0.7 | -1.42 |
| Fgfr3 | 0.71 | -1.41 |
| Ptgs1 | 0.72 | -1.4 |
| Vegfc | 0.74 | -1.35 |
| Fgf1 | 0.76 | -1.31 |
| Tnfaip2 | 0.79 | -1.26 |
| Thbs2 | 0.8 | -1.25 |
| Tgfb3 | 0.82 | -1.22 |
| S1pr1 | 0.84 | -1.19 |
| Pecam1 | 0.84 | -1.19 |
| Ccl2 | 0.85 | -1.18 |
| Ifng | 0.88 | -1.14 |
| Eng | 0.88 | -1.13 |
| Pgf | 0.92 | -1.09 |
| Tgfbr1 | 0.94 | -1.07 |
| Tek | 0.96 | -1.04 |
| Gapdh | 1 | 1 |
| Actb | 1.01 | 1.01 |
| Mmp2 | 1.02 | 1.02 |
| Timp2 | 1.02 | 1.02 |
| Anpep | 1.03 | 1.03 |
| Hsp90ab1 | 1.05 | 1.05 |
| Epas1 | 1.09 | 1.09 |
| Vegfa | 1.09 | 1.09 |
| Ephb4 | 1.15 | 1.15 |
| Mapk14 | 1.17 | 1.17 |
| Nrp1 | 1.2 | 1.2 |
| Cxcl2 | 1.31 | 1.31 |
| Figf | 1.37 | 1.37 |
| Tgfa | 1.38 | 1.38 |
| Hgf | 1.41 | 1.41 |
| Vegfb | 1.44 | 1.44 |
| Npr1 | 1.5 | 1.5 |
| Smad5 | 1.5 | 1.5 |
| Thbs1 | 1.52 | 1.52 |
| Gna13 | 1.54 | 1.54 |
| Pdgfa | 1.57 | 1.57 |
| Hif1a | 1.6 | 1.6 |
| Hprt1 | 1.61 | 1.61 |
| Lama5 | 1.74 | 1.74 |
| Gusb | 1.75 | 1.75 |
| Efnb2 | 1.83 | 1.83 |
| Ereg | 1.87 | 1.87 |

Supplementary Figure 5




Supplementary Figure 6




Supplementary Figure 7